

Short Note

Ethyl 7-Methyl-5-(4-methylphenyl)-3-oxo-2-[[3-(3,4-dichlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]methylidene}-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidine-6-carboxylate

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Abstract: A simple route for synthesis of compound **3** via three component reaction involving ethyl 6-methyl-4-(4-methylphenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**1**), 3-(3,4-dichlorophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde (**2**) and monochloroacetic acid is described. The newly synthesized compound is well characterized by elemental analysis, IR, ¹H-NMR and mass spectral studies.

Keywords: thiazolo[3,2-*a*]pyrimidine; 1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde; multi-component reaction

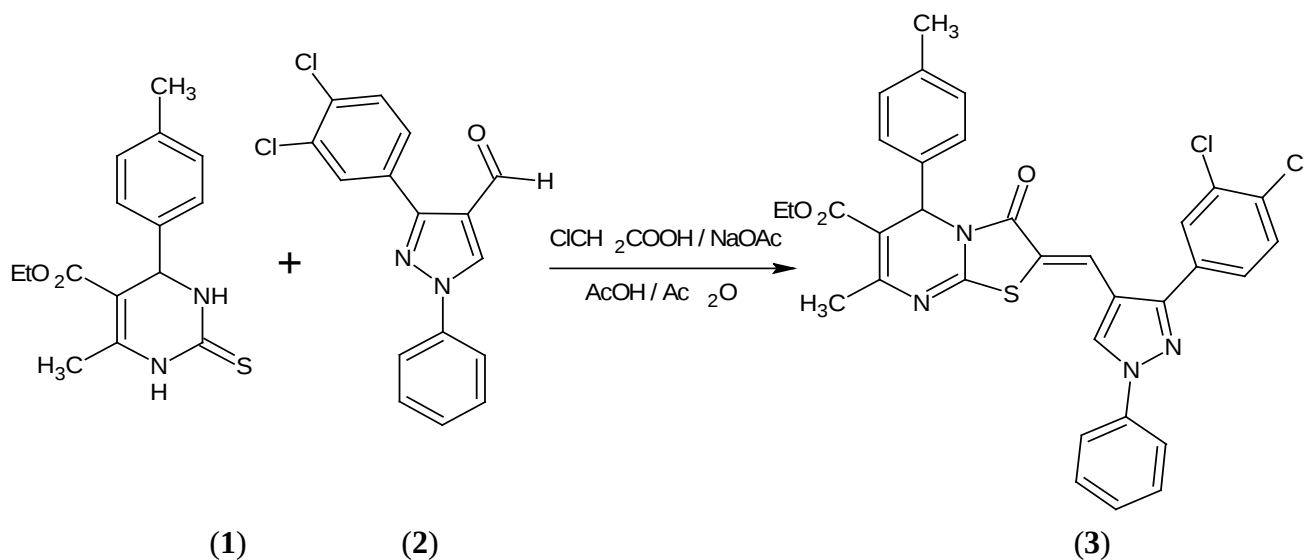
Introduction

Pyrimidine derivatives have been reported to possess a broad spectrum of pharmacological properties including antiviral, antitumor, antibacterial and antihypertensive effects [1,2]. Thiazoles and their derivatives are also found to be associated with various biological activities such as antifungal, antibacterial and anti-inflammatory [3–5]. Thiazolo[3,2-*a*]pyrimidine systems have been known for their unique pharmaceutical and medicinal applications [6,7]. On the other hand the synthesis and the chemistry of the pyrazole nucleus has received much attention during recent decades due to its outstanding biological activities [8–10]. Chemistry and promising biological activities of these derivatives prompted us to synthesize and characterize the title compound.

Results and Discussion

The title compound, ethyl 7-methyl-5-(4-methylphenyl)-3-oxo-2-{[3-(3,4-dichlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]methylidene}-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidine-6-carboxylate (**3**), was synthesized by one pot multi-component reaction involving ethyl 6-methyl-4-(4-methylphenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**1**), 3-(3,4-dichlorophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde (**2**) and monochloro acetic acid in presence of anhydrous sodium acetate in acetic acid-acetic anhydride medium [11–13]. The starting material ethyl 6-methyl-4-(4-methylphenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**1**) was synthesized by Biginelli reaction involving 4-methylbenzaldehyde, ethyl acetoacetate and thiourea in presence of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ catalyst according to the procedure reported in the literature [14]. The other precursor, 3-(3,4-dichlorophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde (**2**) was obtained by Vilsmeier reaction of the corresponding phenylhydrazone [15]. The structure of the newly synthesized compound **3** was established on the basis of elemental analysis, IR, NMR and mass spectral studies. The configuration (*E* or *Z*) at the double bond was not determined.

Scheme 1. Synthesis of ethyl 7-methyl-5-(4-methylphenyl)-3-oxo-2-{[3-(3,4-dichlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl]methylidene}-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidine-6-carboxylate.



The ^1H -NMR spectrum of compound **3** was verified on the basis of their chemical shifts, multiplicities, and coupling constants. A triplet appeared at δ 1.09 ppm and quartet at δ 3.99 ppm confirmed the presence of methyl and methylene protons of the ester chain. Two characteristic singlets appeared at δ 5.95 ppm and δ 8.79 ppm was due to the proton present in the pyrimidine and pyrazole ring respectively. Benzylidene proton appeared as a singlet at δ 7.48 ppm. Two singlets observed at δ 2.23 ppm and δ 2.31 ppm indicated the presence of two methyl group present in the structure. A multiplet observed in the region δ 7.11–8.02 ppm for 12 aromatic protons present in the title compound. In the IR spectrum, the sharp absorption band appeared at 1653 cm^{-1} was due to carbonyl group of the ester and other sharp band appeared at 1614 cm^{-1} was due to the cyclic carbonyl group. LCMS and ^{13}C -NMR spectrum was in complete agreement with the title compound.

Experimental

Melting points were determined by open capillary method and are uncorrected. The IR spectrum (in KBr pellets) was recorded on a Shimadzu FT-IR spectrophotometer. ^1H -NMR spectrum was recorded on a Bruker AMX-400 (400 MHz) spectrophotometer using TMS as an internal standard. ^{13}C -NMR spectrum was recorded for approximately 0.03 M solutions in $\text{DMSO-}d_6$ at 100 MHz with TMS as internal standard. The mass spectrum was recorded on a Agilent 1200 series LC and Micromass zQ spectrometer. Elemental analysis was carried out by using VARIO EL-III (Elementar Analysensysteme GmbH). The purity of the compounds was checked by thin layer chromatography (TLC) on silica gel plate using n-hexane and ethyl acetate (4:1, v/v).

A mixture of ethyl 6-methyl-4-(4-methylphenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **1** (2.90 g, 10 mmol), 3-(3,4-dichlorophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde **2** (3.17 g, 10 mmol), monochloroacetic acid (1.41 g, 15 mmol) and anhydrous sodium acetate (2 g) was dissolved in glacial acetic acid (25 mL)-acetic anhydride (20 mL) mixture and were heated to reflux for 6 h. The reaction mixture was cooled to room temperature and poured into crushed ice with vigorous stirring. The precipitated solid was filtered under suction, washed with cold water and recrystallized from ethanol. Yield was 5.31g (84%).

Melting point: 105–107 °C.

LCMS: m/z = 629(M^+), 631($\text{M}^+ + 2$), 633 ($\text{M}^+ + 4$).

IR (KBr): ν_{max} (cm^{-1}), 2922, 2980 (C-H), 1712 (C=O ester), 1614 (cyclic C=O), 1552 (C=N and aromatic C=C), 1159 (C-O), 756 (C-Cl).

^1H -NMR (400 MHz, $\text{DMSO-}d_6$): δ ppm, 1.09 (t, 3H, J = 7 Hz, ester- CH_3), 3.99 (q, 2H, J = 7.12 Hz ester- CH_2), 2.31 (s, 3H, CH_3), 2.23 (s, 3H, Ar- CH_3), 5.95 (s, 1H, pyrimidine-CH), 7.48 (s, 1H, CH), 7.11–8.02 (m, 12H, Ar-H), 8.79 (s, 1H, pyrazole CH).

^{13}C -NMR (100 MHz, $\text{DMSO-}d_6$): δ ppm, 13.88 (ester CH_3), 20.67 (CH_3), 22.47 (CH_3), 54.72 (ester CH_2), 60.14 (CH), 108.75, 115.56, 119.35, 119.42, 122.24, 127.38, 127.69, 128.32, 128.71, 129.21, 129.58, 130.08, 131.13, 131.75, 131.79, 131.88, 137.47, 138.00, 138.49, 150.97, 151.01, 155.14, 163.91, 164.82 (C=O).

Elemental analysis: Calculated for $\text{C}_{33}\text{H}_{26}\text{Cl}_2\text{N}_4\text{O}_3\text{S}$, C, 62.96%; H, 4.16%; N, 8.90% Found: C, 62.90%; H, 4.11%, N, 8.85%.

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